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I hereby certify that, on the date indicated above I deposited this paper or fee with the U.S. Postal Service and that it was addressed for delivery to the Commissioner of Patents and Trademarks, Washington, D.C. 20231 by "Express Mail Post Office to Addressee" service.

A. DiLullo
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2427/1E988-US1

**A TUMOR SUPPRESSOR PROTEIN INVOLVED IN DEATH
SIGNALING, AND DIAGNOSTICS, THERAPEUTICS,
AND SCREENING BASED ON THIS PROTEIN**

The research leading to this invention was supported in part by National Institutes of Health grant no. CA 67938 and National Institutes of Health Cancer Center Core grant no. CA 21765.

FIELD OF THE INVENTION

The present invention relates to identification of tumor suppressor activity of a protein, and to related diagnostic and therapeutic compositions and methods. The discovery of this tumor suppressor activity provides screening targets as well, particularly screening for compounds that overcome gene inactivation that results from genomic methylation of the promoter.

BACKGROUND OF THE INVENTION

The cysteine proteases caspase-8 (alternatively named FLICE1/MACH1), caspase 9 (alternatively named Apaf 3/Mch6) and caspase-10 (alternatively named FLICE2/MACH 2) are related proteins that share homology with the prototypic member of the larger caspase gene family, interleukin-1 β -converting enzyme (ICE)/caspase 1 (Muzio *et al.*, J. Biol. Chem., 1998, 273:2926-2930; Boldin *et al.*, Cell, 1996, 85:803-815; Srinivasula *et al.*, J. Biol. Chem., 1996, 271:27099-27106; Orth *et al.*, J. Biol. Chem., 1996, 271:20977-20980; Scaffidi *et al.*, EMBO J.,

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3. ☐ Formal drawings, _ sheets (Figs.)
☒ Informal drawings, fourteen (14) sheets (Figs. 1-8)
4. ☐ Assignment for recording to:
5. ☐ Verified Statement Claiming Small Entity Status
6. ☐ Check in amount of \$ 00, (\$ filing; \$ recording; \$ surcharge)
(See attached Fee Computation Sheet)
7. ☐ Preliminary Amendment.

8. ☒ Please amend the description by inserting the following paragraph after the line containing the title on page 1:

*from
paper
12/31/99*
INS
X This patent application claims the priority of U.S. provisional patent application No. 60/114,308, filed December 31, 1998, which is incorporated herein by reference. X

Priority is claimed for this application, corresponding application/s having been filed as follows:

Country:
Number:
Date:

The priority documents ☐ are enclosed
☐ will follow.

Respectfully submitted,



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